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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/322,348	10/13/94	BRENNER S	CBD1

18M1/0226

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EXAMINER	
PRIEBE S	

ART UNIT	PAPER NUMBER
1805	7

DATE MAILED: 02/26/96

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/322,348	Applicant(s) Brenner, S.
	Examiner Scott D. Priebe	Group Art Unit 1805

☒ Responsive to communication(s) filed on *Feb 7, 1995* .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1 and 3-10* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1 and 3-10* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *11/17/94*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

X Notice to comply w/ Sequence Rules

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Part III DETAILED ACTION

Election/Restriction

Claim 1 is generic to a plurality of disclosed patentably distinct species comprising methods of sorting polynucleotides, classified in Class 435, Subclass 25.4; methods of sorting peptides, classified in Class 530, Subclasses 344, 413; and methods of sorting compounds of the form $-(M-L)_n-$, classified in Class 435, Subclass 6. Applicant is required under 35 U.S.C. § 121 to elect a single disclosed species, even though this requirement is traversed.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. § 103 of the other invention.

During a telephone conversation with Stephan Macevicz on 2/6/96 a provisional election was made with traverse to prosecute claim 1-13 restricted to the species of methods of sorting peptides. Affirmation of this election must be made by applicant in responding to this Office action.

Applicant's amendment to claim 1 and cancellation of claims 2 and 11-13 in the Preliminary amendment filed 2/7/96 renders the election of species requirement moot.

Drawings

This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. §§ 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821 through 1.825 for the following reasons:

Nucleotides sequences appear in the specification which are not listed on the Sequence Listing, for example: at page 17, line 36; page 18, line 17; page 27, lines 9, 32 and 35; page 28, lines 33 and 36; and page 29, lines 1 and 4. Nucleotide sequences appearing in the specification are not identified in the text of the description by the assigned SEQ ID NO.

Applicants are required to comply with all of the requirements of 37 C.F.R. §§ 1.821 through 1.825. *Any* response to this Office Action which fails to meet *all* of these requirements will be considered non-responsive. The nature of the noncompliance with the requirements of 37 C.F.R. §§ 1.821 through 1.825 did not preclude the examination of the application on the merits, the results of which are communicated below.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to adequately teach how to make and /or use the invention, i.e. failing to provide an enabling disclosure.

The specification does not describe the sorting of peptides of a population of peptides or the nature or origin of the peptides to be sorted, either by general guidance or by working example. No potential applications or situations requiring or facilitated by the sorting of peptides is mentioned.

The only reference to peptides in the context of the invention occurs at page 15, lines 9-14 of the specification which states:

> "Peptides are another preferred class of molecules to which tags of the invention are attached. Synthesis of peptide-oligonucleotide conjugates for use in the invention is taught in...".

followed by references to non-patent literature. Since no description of the intended peptide-oligonucleotides are described in the specification, the information contained in

these references is deemed to be essential for the practice of the invention. Since the references are not U.S Patents or allowed U.S. Patent applications, their contents may not be incorporated by reference. It is not clear from the cursory mention of these references, what information relevant to the invention, other than the synthesis of the conjugates, is contained in these references. Truffert et al. and de la Torres et al. describe methods of synthesizing specific oligonucleotide-peptide conjugates designed for specific purposes, in which the identity of the peptide and oligonucleotide moieties are known and each moiety has a specific intended function unrelated to sorting. First, the peptide is synthesized on a solid support then the oligonucleotide is synthesized onto the peptide. It is not clear what purpose would be served by sorting known conjugates or what population of peptides they would be sorted from. The references do not disclose the sorting of peptides based on the attached oligonucleotides or suggest any applications for the claimed sorting method.

The specification does not teach how to make the invention. If the population of peptides contemplated is from a combinatorial library, which is not described in the specification, it is not clear how the oligonucleotide tags would be attached to the peptides. Would the subunits of the tags be added individually onto the peptide or would a complete

oligonucleotide tag be added to a peptide. The method claimed requires that identical peptides be attached to the same oligonucleotide tag and that different peptides be attached to different oligonucleotide tags. There is no description as to how this would be accomplished. If the peptide population were synthesized positionally on arrays, they would already sorted, regardless of whether tags were subsequently attached. If the peptides were synthesized on beads or microparticles using a split-synthesis strategy, addition of the tags to the completed peptides would be random. Each population of identical peptides would be made up of subpopulations comprising each of the tags used. Sorting the population of all peptides by hybridization would simply result in isolated subpopulations of different peptides conjugated to the same oligonucleotide tag.

The specification does not teach how to use the invention, since no applications of the sorting method are described for peptides. No relevant prior art has been cited which suggests an application for the invention. Sorting of peptide libraries disclosed in the prior art, whether encoded or not, is accomplished by affinity methods utilizing the desired antiligand for which a peptide ligand is sought. Tags, e.g oligonucleotides, are then used to determine the identity of the successful peptide ligand, rather than resorting to sequencing the peptide.

Further, claim 1 lacks an essential method step. The claim recites sorting the peptides by hybridizing the tags with their respective complements. It is not clear from the specification or the prior art cited or of record how merely hybridizing the complement to the tag would effect sorting. Sorting would entail a physical separation of the different peptides from each other. Simply hybridizing a free tag complement to the tag would not accomplish any physical separation unless the different tag complements were themselves already physically separated. The specification teaches that sorting is accomplished by having the tag complements attached to a solid support, wherein each specific complement within the repertoire of complements is attached to different discrete regions of an array on a planar substrate or attached to different microparticles. This part of the objection could be obviated by incorporating the limitations of claim 3 into claim 1.

The specification and prior art of record do not describe how to make or use the invention as claimed. In the absence of such information, it would be left to the skilled artisan to determine an application for such a method and develop the necessary methodology to carry out that application. This would require excessive experimentation involving inventive activity with no predictability of success. As a result, the invention as claimed represents an invitation to experimentation.

Claim Rejections - 35 USC § 112

Claims 1 and 3-10 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification. It has been assumed that claims 3-10 are dependent on claim 1 (see rejection of claims 3-10 under 35 USC 112, second paragraph).

Claims 1, 3-10 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

Claim 1 is unclear for recitation of "... peptide or ... subpopulation of peptides". Does "sorting "a peptide" mean that a single peptide molecule is sorted; and what constitutes a "subpopulation of peptides", are the members of the subpopulation identical or different? The specification does not describe what is meant by subpopulation of peptides. It is suggested that in the preamble, "sorting a peptide or subpopulation of peptides in a population of peptides" be replaced with --sorting peptides of a population of peptides-- and elsewhere in the claim "peptide or ... subpopulation of peptides" be replaced with --peptides--.

Claims 3-10 are indefinite for depending on cancelled claim 2.

Claims 3-4 are vague for recitation of "a single kind of said complement" in claim 3. It is not clear what property of the complement "a single kind" refers to. Does it refer to the sequence of the complement or some other property such as the internucleotide linkage or RNA vs. DNA? In light of the specification, it appears that "kind" refers to the sequence of the complement; if so this should be recited in claim 3.

Claims 6-10 are indefinite as claims 6 and 7 are unclear and fail to distinctly claim the invention as described in the specification. The specification at page 4, lines 17-26 and page 16, lines 16-25 describes the embodiment wherein the complements of the tags are attached to planar substrates in an array. As disclosed, each position of the array is uniformly coated with one type of complement having a particular sequence and the population of regions contains the repertoire of complements, i.e. each region is coated with a different complement. It is not clear from the specification whether "uniform populations" recited in claims 6 and 7 refers to a uniform density of complements within each region or whether each region has attached within it a single type of complement. It is also unclear in claim 6, whether all of the regions have the same type of complement or each of the regions has a different kind of complement, as recited in claim 7. Also, "said uniform populations of different kinds of said complements" recited in

claim 7 is confusing and lacks antecedent basis. It is suggested that claim 6 be amended to more clearly recite the limitations intended and include the limitation of claim 7.

Claims 7-10 are indefinite for recitation of "said plurality" in claim 7. It is not clear whether "said plurality" refers to "plurality of subunits" recited in claim 1 or "plurality of discrete non-overlapping surface regions" recited in claim 6.

Claims 7-10 are vague for recitation of "different kinds of said complement" in claim 7. It is not clear whether "different kinds" refers to complements differing in their sequence or differing in some other way, such as having different types of internucleotide linkages. In light of the specification, it appears that the complements in the different regions differ in their sequence. If so, this should be recited in the claim.

Conclusion

No claims are allowed.

Certain papers related to this application may be submitted to Art Unit 1805 by facsimile transmission. The FAX number is (703) 308-4312. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (703) 308-7310. The examiner can normally be reached on Monday through Friday from 9 AM to 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mindy Fleisher, Ph.D., can be reached on (703) 308-0407.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SDP

Scott D. Priebe, Ph.D.
Examiner

February 16, 1996

Mindy B. Fleisher

MINDY FLEISHER
SUPERVISORY PATENT EXAMINER
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